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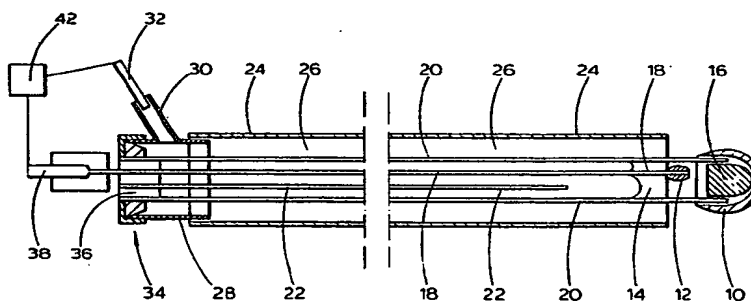
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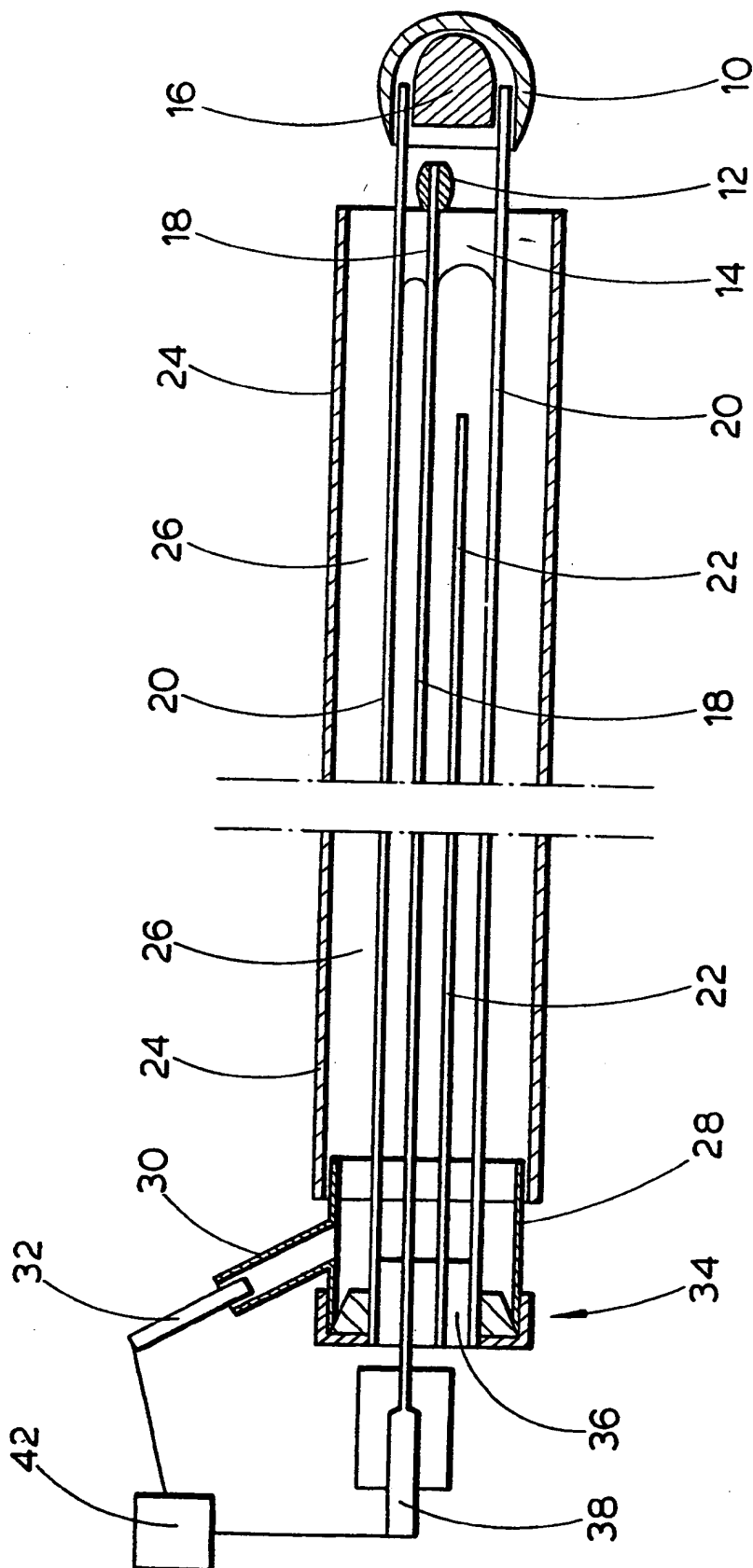
(54) Device for measuring ionic concentration

(57) A device for measuring the concentration of a specific ion, particularly a pH measuring device, comprises a membrane 10 permeable to the ion a measuring electrode 12 connected to an insulated electric conductor 18, and a reference electrode 32. A tube 24 surrounds the electrical conductor and is filled with electrolyte which may be gelled, to provide connection to the reference electrode and to shield the conductor from electrical interference. Means 42 are provided for amplifying the P.D. developed between the measuring and reference electrodes. The device is suitable for use as a catheter tip pH electrode for the accurate and continuous measurement of small pH changes in the arteries and veins of man.



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SPECIFICATION

Device for measuring ionic concentration

5 This invention relates to a device for measuring the concentration of an ion in an electrically conducting medium. Devices of this kind are known, and are based on the use of a membrane permeable only to the ion whose concentration is being measured.

10 Thus for example, one commercially available membrane is permeable only to potassium ions; another is permeable only to calcium ions; and yet another is permeable only to hydrogen ions, and forms the basis of well known pH electrodes. Such
15 devices find utility in medicine, both for *in vitro* and *in vivo* use, and also in industry, and the present invention is useful in both these fields.

A particular problem that has confronted the medical profession has been the measurement of pH *in vivo*. The standard glass pH electrodes cannot be used *in vivo* because they promote blood clotting and are brittle, and it has therefore been general practice to withdraw a sample of blood or other body fluid for pH measurement. In 1976, Le Blanc et al
20 described a polymeric hydrogen ion permeable membrane (Journal of Applied Physiology, 40, 644 to 647). Their polymer comprised three parts of para-octadecyloxy meta - chlorophenylhydrazone mesoxalonitrile (a hydrogen ionophore) to 1,000
30 parts of the block polymer, 60% polysiloxane/40% poly(bisphenol A carbonate). By casting this copolymer mixture directly onto a silver chloride electrode, the General Electric Company of America have produced a pH measuring device. However, the
35 thickness of the silver wire required to achieve an adequate electrical contact with the polymeric membrane makes the device rather stiff and suitable for insertion into superficial body sites only. Also, the device does not include a reference electrode,
40 which accordingly has to be inserted separately. There is accordingly a need for a device of this kind but which can be inserted into any accessible part of the body and which includes a reference electrode.

The present invention provides a device for
45 measuring the concentration of an ion in an electrically conducting medium, comprising a membrane permeable to the ion, a measuring electrode in electrical contact with an inner surface of the membrane and with an insulated electrical conductor, a tube
50 surrounding the conductor with the measuring electrode protruding from a first end thereof, the tube to be filled with electrolyte providing connection with a reference electrode, the outer surface of the membrane and the first end of the tube to be positioned in
55 the medium to be measured, and, at the end of the tube remote from the measuring electrode, means for amplifying the potential difference between the measuring electrode and the reference electrode.

The invention will be further described with reference to the accompanying drawing which is a diagrammatic cross-section, not drawn to scale, of a
60 device for measuring pH deep in the human body.

Referring to the drawing, the device comprises a membrane 10 of the polymeric material referred to
65 above which is permeable to hydrogen ion. This polymer has the advantage over glass that it does not have a strong blood clotting tendency and is strong and flexible. A silver chloride electrode 12 is in electrical contact with the inner surface of the
70 membrane 10 via a buffered aqueous solution 14 and a porous ceramic plug 16. The silver chloride electrode 12 is the tip of an insulated silver wire 18, and has been formed by stripping the insulation (not shown) from the last centimetre or so of the wire and electrolytically depositing silver chloride on the bare
75 end in dilute hydrochloric acid. The insulated silver wire 18 and silver chloride electrode 12 are contained in a tubule 20, suitably of polyethylene or other inert plastics material.

80 The silver wire 18 is 0.1 mm. diameter, and the polyethylene tubule 20 is 0.9 mm. external diameter. A stainless steel stylet 22 is also provided in the tubule to impart a desired degree of rigidity and springiness. The buffered solution 14 comprises
85 sodium chloride (58 mmol/l), sodium citrate (38 mmol/l) and citric acid (19 mmol/l). This buffer solution occupies the distal 5 mm. of the tube 20, and is held in position by surface tension. The stylet 22 is not in electrical contact with the buffer solution 14. A
90 tube 24 surrounds the tubule 20 with the measuring electrode 12 protruding from one end thereof. The tube 24 is filled with electrolyte 26 and provides connection with a reference electrode 32. The tube is a standard commercially available catheter, suitably
95 one made of woven Dacron (a terylene polymer), and the electrolyte is an aqueous solution of sodium chloride (145 mmol/l) and heparin (1,000 units/l). The electrolyte 26 serves the additional important function of screening the silver wire 18 from electrical
100 interference.

Fixed in the end of the tube 24 remote from the measuring electrode 12 is a side arm adaptor 28. A supply (not shown) of electrolyte 26 is introduced into the tube 24 via the side arm 30 where there is
105 also provided an electrical connection for the reference electrode 32. This end of the tube 24 is stoppered by means of a screw threaded plug 34 which can be loosened to permit the tubule 20 to slide along the tube 24. The end of the tubule 20 is plugged with silicone rubber 36 and provided with an
110 electrical connection 38 for the measuring electrode within a protective block 40 of epoxy resin. Means 42 are provided for amplifying the potential difference between the measuring electrode 12 and the reference electrode 32.

The first step in manufacturing this device is to strip the insulation from an end of the fine silver wire 18 and coat the bare end with silver chloride. This wire is when threaded, together with the stylet 22
120 down the tubule 20 until the measuring electrode 12 is just short of the end. The buffering solution 14 is sucked into the tubule and a porous ceramic plug 16 is inserted in the end of the tubule. The membrane 10 is dip-cast from a solution in methylene chloride

The drawing(s) originally filed were informal and the print here reproduced is taken from a later filed formal copy.

of the hydrogen ion permeable copolymer. Dipping and evaporation of solvent are repeated until a suitably thick coating is achieved. A dry atmosphere and a temperature of 4°C is preferred to produce clear membranes without bubbles. The other end of the tubule 20 is plugged with silicone rubber 36. An electrical socket is joined to the protruding end of the silver wire 18 and the joint protected by means of the block 40 of epoxy resin. After sterilisation by immersion in glutaraldehyde, the tubule is ready for use.

The side arm adaptor 28, which is a standard commercially available item of equipment, is fitted to one end of the catheter 24. The sterile tubule 20 is inserted into the catheter through the screw threaded plug 34 and slid along the catheter until the membrane 10 is just inside the other end of the tube 24. The stylet 22 assists in sliding the tubule along the catheter; without the stylet, the tubule would tend to buckle. Then the catheter is inserted in the usual way into a vein or artery in the patient's arm or leg and eased along until the tip is in the required position. If there is doubt about the position of the tip, a radio-opaque "dye" can be pumped down the catheter and an X-ray picture taken. Once the catheter is in position, the plug 34 is loosened and the tubule 20 is eased forward until it extends about 1 cm. beyond the end of the catheter. Since the stylet does not extend up to the end of the tubule, the distal end of the tubule is quite soft and flexible and can be pushed forward without causing damage. The crew threaded plug 34 is tightened and a slow stream of saline and heparin pumped through the catheter via the side arm 30. The electrodes 32, 38 are connected across a high-input impedance amplifier, and electrical isolation is achieved with a DC voltage source and an optical isolator or by other techniques such as telemetry.

In tests on dogs, a device made according to this design had an output of 58 to 59 milli volts per unit of pH, that is to say greater than 95% of that predicted by the Nernst relationship. The response was the same for changes of pH achieved by alterations of carbon dioxide pressure and the bicarbonate/chloride ion ratio. The output of the electrode was insensitive to physical pressure, osmotic pressure or oxygen pressure and was unaltered by changes (mmol/l) of sodium (100 to 200), potassium (0 to 10), calcium (0 to 10) or magnesium (0 to 10). The response time was less than 300 milli seconds. The resistance of the electrodes was approximately 10⁸ Ohms. Excellent noise-free records have been obtained in veins *in vivo*. In arteries a small signal occurred in time with the heartbeat. It was equivalent to less than 0.01 pH units and appeared to be related to movement of the catheter tip. The electrode was capable of detecting changes of pH as small as 0.005 units.

Clinical studies undertaken in patients undergoing routine cardiac catheterisation have shown that pH can be recorded continuously in central arteries and veins. Breath by breath oscillations of pH have been demonstrated in the central aorta and pulmonary veins. Changes in coronary sinus pH can also be demonstrated following the induction of angina pectoris by atrial pacing in patients with coronary artery

disease.

The device has the advantages that it is sensitive, has an exceptionally fast response, uses a standard cardiac catheter and allows continuous monitoring pH anywhere in the central arteries or veins of man. The device may be inserted, for example, into the coronary sinus, superior vena cava, the pulmonary artery, the aorta or other arteries, the femoral vein, the stomach or the urinary tract. With trivial modification, a shorter electrode (5 cm. long, 0.5 mm. diameter) can be made which has a pH sensitive tip and is suitable for the measurement of muscle or tissue pH. By a suitable change of the material of the membrane 10, the device can be modified to measure the concentration of any desired ion, such as potassium or calcium.

Numerous variations are possible within the scope of the invention. Thus it would be possible to use a ptfe catheter, although these are known to be less manoeuvrable than woven Dacron catheters. It would be possible to use a tubule of some material other than polyethylene, for example polyvinylchloride, although we have experienced difficulty in pushing stylets down PVC tubes. It would be possible to dispense with the buffer solution 14 and bring the measuring electrode 12 into electrical contact with the inner surface of the membrane 10; this is not preferred for cardiac use, but might be more convenient for superficial body use or for industrial purposes. When the device is being used *in vivo*, it is convenient to use sodium chloride as the electrolyte 26; when the device is intended for industrial use, no such limitation exists, and any suitable electrolyte may be used. Moreover, it is not necessary to pump the electrolyte through the tube 24, it might more conveniently be provided in the form of a gel. For industrial use it may be more convenient to make the tube 24 rigid.

CLAIMS

1. A device for measuring the concentration of an ion in an electrically conducting medium, comprising a membrane permeable to the ion, a measuring electrode in electrical contact with an inner surface of the membrane and with an insulated electrical conductor, a tube surrounding the conductor with the measuring electrode protruding from a first end thereof, the tube to be filled with electrolyte providing connection to a reference electrode, the outer surface of the membrane and the first end of the tube to be positioned in the medium to be measured, and, at the end of the tube remote from the measuring electrode, means for amplifying the potential difference between the measuring electrode and the reference electrode.
2. A device as claimed in claim 1 wherein the membrane is permeable to hydrogen ions.
3. A device as claimed in claim 1 or claim 2 wherein the measuring electrode is present in a tubule, one end of which is capped with the membrane.
4. A device as claimed in claim 3 wherein the tubule also contains a stiffener.
5. A device as claimed in any one of claims 1 to 4, wherein the tube is a catheter to be filled with an aqueous solution of sodium chloride.

6. A device substantially as hereinbefore described with reference to, and as illustrated in, the accompanying drawing.

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